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Characteristics, outcomes and risk factors for mortality of 522 167 patients hospitalised with COVID-19 in Brazil: a retrospective cohort study

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ABSTRACT

Objective To provide a comprehensive description of demographic, clinical and radiographic characteristics; treatment and case outcomes; and risk factors associated with in-hospital death of patients hospitalised with COVID-19 in Brazil.

Design Retrospective cohort study of hospitalised patients diagnosed with COVID-19.

Setting Data from all hospitals across Brazil.

Participants 522 167 hospitalised patients in Brazil by 14 December 2020 with severe acute respiratory illness, and a confirmed diagnosis for COVID-19.

Primary and secondary outcome measures Prevalence of symptoms and comorbidities was compared by clinical outcomes and intensive care unit (ICU) admission status. Survival was assessed using Kaplan Meier survival estimates. Risk factors associated with in-hospital death were evaluated with multivariable Cox proportional hazards regression.

Results Of the 522 167 patients included in this study, 56.7% were discharged, 0.002% died of other causes, 30.7% died of causes associated with COVID-19 and 10.2% remained hospitalised. The median age of patients was 61 years (IQR, 47–73), and of non-survivors 71 years (IQR, 60–80); 292 570 patients (56.0%) were men. At least one comorbidity was present in 64.5% of patients and in 76.8% of non-survivors. From illness onset, the median times to hospital and ICU admission were 6 days (IQR, 3–9) and 7 days (IQR, 3–10), respectively; 15 days (IQR, 9–24) to death and 15 days (IQR, 11–20) to hospital discharge. Risk factors for in-hospital death included old age, Black/Brown ethnoracial self-classification, ICU admission, being male, living in the North and Northeast regions and various comorbidities. Age had the highest HRs of 5.51 (95% CI: 4.91 to 6.18) for patients≥80, compared with those ≤20.

Conclusions Characteristics of patients and risk factors for in-hospital mortality highlight inequities of COVID-19 outcomes in Brazil. As the pandemic continues to unfold, targeted policies that address those inequities are needed to mitigate the unequal burden of COVID-19.

Strengths and limitations of this study

- ► The strength of this study is that it leverages Brazil's established national Influenza Epidemiological Surveillance Information System data to present comprehensive characteristics, clinical course and risk factors for COVID-19 in-hospital deaths across Brazil.
- ► Administrative records lack details available in hospital medical records and may have accuracy and completeness problems.
- ► We did not have access to laboratory results other than COVID-19 tests (eg, complete blood count) that would allow for a better characterisation of the clinical course of the disease.
- ► COVID-19 deaths at home likely follow a different clinical course than deaths in the hospital and are not included in this analysis.
- ► In-hospital deaths due to COVID-19 are likely underreported and are limited by the testing protocol and capacity of each hospital.

INTRODUCTION

On 11 March 2020, the WHO declared COVID-19 as a pandemic. Caused by the novel coronavirus SARS-CoV-2, it emerged in China and quickly spread across the country and beyond. As of 16 February 2021, it was present in 223 countries and territories, with 108 822 960 confirmed cases and 2 403 641 confirmed deaths.[1] Brazil recorded the first confirmed COVID-19 case on 26 February 2020 and the first death on 12 March, both in São Paulo State. In 24 days, the disease had spread to all Federal Units. As of 16 February 2021, 9 834 513 cases (9% of worldwide cases) and 239 245 deaths (10% of worldwide deaths) had been reported in Brazil, the second-highest in the world, behind only the USA. These numbers are underestimated since most mild cases are not being tested and thus are not likely to be reported, and some deaths may be reported with ill-defined causes, or not reported at all.

Brazil has a comprehensive health information system,[2] with the systematic collection of births, deaths, hospitalisations and diseases

of mandatory notification, among others. However, a complete and linked registry of records combining data from ambulatory and inpatient care, laboratory and radiologic results and outcome of the disease is not available. Therefore, there is limited information on the course of the disease for every case reported in Brazil.

Currently, the most detailed data available in Brazil refer to hospitalisations due to severe acute respiratory illness (SARI). Here, we use these data to provide a comprehensive description of demographic, clinical and radiographic characteristics, treatment, case outcome and risk factors associated with in-hospital death of patients hospitalised with SARI with a confirmed diagnosis for COVID-19, as of 14 December 2020. We analyse the largest retrospective number of cases (n=522 167) and we assess whether the Brazilian case is comparable to patterns previously described for other countries.

METHODS

Data sources

We used deidentified records from the Influenza Epidemiological Surveillance Information System (*Sistema de Informação de Vigilância Epidemiológica da Gripe, SIVEP-Gripe*, in Portuguese), an information system of the Ministry of Health that captures all notifications of SARI hospitalisations in both public and private hospitals. The system is updated daily, and every 2 weeks, a new data set is made publicly available (https://opendatasus.saude.gov.br/nl/dataset). Here, we analysed records as of 14 December 2020 (n=1 029 684 notifications), after 15 419 duplicate records were removed by the Ministry of Health. Each record has data on patient's age, sex, place of residence and of hospitalisation, ethnoracial self-classification,[3] pregnancy status, comorbidities and symptoms; drug treatment; radiologic test results; and dates of illness onset, hospitalisation, ICU admission and outcome (death, release, still hospitalised). We considered only records of patients hospitalised with a confirmed diagnosis for COVID-19 (n=522 167). Diagnosis followed the Ministry of Health guidelines.[4]

Statistical analysis

Characteristics of inpatients were summarised in three groups: demographic, clinical and radiographic and treatment and outcomes. Medians and IQR ranges were used to describe continuous variables, and counts and percentages to describe categorical variables. Differences between inpatients that needed and did not need ICU admission and those that survived and did not survive were assessed by Whitney U, χ^2 or Fisher's exact test, as appropriate. No data imputation was performed for missing data (see online supplemental table 1 for information on data completeness).

Survival curves of inpatients at 60 days of hospitalisation by age, sex, ethnoracial self-classification, region and ICU admission were estimated using the Kaplan-Meier estimator and compared with the log-rank test. Factors associated with inpatient death were identified by univariable and multivariable logistic regression (excluding from the analysis those that remained hospitalised). Considering time to death as the outcome, HRs were estimated using Cox proportional-hazards models. Based on previous studies[5–7] and on our available information, covariates included in both logistic and Cox models were age (0–19, 20–39, 40–59, 60–69, 70–79 and 80 or more years), sex, ethnoracial self-classification (White, Black/Brown, other, not reported), region (North—where Amazonia is located, Northeast, South, Southeast—where the cities of São Paulo and Rio de Janeiro are located and Center-West), comorbidities (diabetes, asthma, chronic liver disease, chronic neurological disease, chronic lung disease, immunodeficiency and chronic kidney disease), obesity and ICU admission. The variable ethnoracial self-classification was missing in 23.1% of the records, and we added those as a separate category (not reported). Distances between municipalities of residence and hospitalisation were calculated in ArcMap, V.10.6 (ESRI, Redlands, CA, USA). All analyses were performed in Stata, V.15.1 (Stata Corp., College Station, TX, USA), and R V.4.0.0 (RStudio Team, Boston, MA, USA).

Patient and public involvement

Our analysis used administrative records, and thus study participants were not involved in the design of the study. Public involvement was achieved through collaboration with the Ministry of Health, with whom we defined the research questions to fill in knowledge gaps and inform decision-making. Results were discussed and shared with the Ministry, and their wide dissemination with public health officials, researchers and through the media will reach the broader public.

RESULTS

As of 14 December 2020, 522 167 patients had been hospitalised with confirmed COVID-19 since the beginning of the epidemic in Brazil. Of those, 296 002 (56.7%) were discharged, 1004 (0.002%) died of other causes, 160 495 (30.7%) died of causes associated with COVID-19, 53 503 (10.2%) remained hospitalised. Clinical outcome was unknown for 11 126 (2.1%) patients (table 1). The cumulative curve of hospital admissions (online supplemental figure 1) shows the fast increase in severe cases that required hospitalisation, following the steep increase in COVID-19 transmission in Brazil since the end of March. The median age of patients was 61 years (IQR, 47–73), and much higher for non-survivors, 71 years (IQR, 60–80), as shown by the age distribution in figure 1A,B. Patients aged 60 years or more represented 50.1% of hospitalisations, 59.0% of ICU admissions and 74.0% of deaths associated with COVID-19. Patients were mostly males (56.0%) and from the Southeast region (49.3%). Among females, 2.5% were pregnant or puerperal at the time of hospitalisation, and 7.5% of those died in the hospital. A total of 172 473 (33.0%) patients with median

Table 1 Demographic characteristics of patients

Characteristic	All patients (n=522 167)*	ICU admission (n=172 473)	Non-ICU admission (n=293 384)	Not reported (n=56 310)	P value	Survivor and non-COVID-19 death (n=297 043)	Non-survivor (n=160 495)†	Still in the hospital (n=53 503)	P value
Age									
Median (IQR)—years	61 (47–73)	65 (52–76)	59 (45–72)	61 (47–74)	<0.001	56 (42–68)	71 (60–80)	60 (46–72)	<0.001
Distribution, number (%)					<0.001				<0.001
0–19	13 136 (2.5)	3211 (1.9)	8517 (2.9)	1408 (2.5)		9994 (3.4)	985 (0.6)	1628 (3.0)	
20–39	71 728 (13.7)	16 978 (9.8)	46 823 (16.0)	7927 (14.1)		54 889 (18.5)	7299 (4.6)	7814 (14.6)	
40–59	170 266 (32.6)	50 445 (29.3)	101 922 (34.7)	17 899 (31.8)		114 769 (38.6)	33 405 (20.8)	18 196 (34.0)	
60–69	108 416 (20.8)	39 362 (22.8)	57 404 (19.6)	11 650 (20.7)		56 788 (19.1)	38 044 (23.7)	11 352 (21.2)	
70–79	90 800 (17.4)	35 944 (20.8)	44 943 (15.3)	9913 (17.6)		38 304 (12.9)	41 883 (26.1)	8942 (16.7)	
≥80	67 808 (13.0)	26 530 (15.4)	33 769 (11.5)	7509 (13.3)		22 303 (7.5)	38 872 (24.2)	5570 (10.4)	
Sex, number (%)					<0.001				<0.001
Male	292 570 (56.0)	100 399 (58.2)	161 377 (55.0)	30 794 (54.7)		163 967 (55.2)	92 376 (58.6)	30 146 (56.3)	
Female	229 513 (44.9)	72 060 (41.8)	131 964 (45.0)	25 489 (45.3)		133 028 (44.8)	68 101 (42.4)	23 345 (43.6)	
Pregnant, number (%)	4441 (1.9)	802 (1.1)	3249 (2.5)	390 (1.5)	<0.001	3603 (2.7)	230 (0.3)	469 (2.0)	<0.001
Puerperal, number (%)	1350 (0.6)	426 (0.6)	850 (0.6)	74 (0.3)	<0.001	965 (0.7)	204 (0.4)	148 (0.6)	<0.001
Ethnoracial, number (%)					<0.001				<0.001
White	196 035 (37.5)	67 619 (39.2)	114 339 (39.0)	14 077 (25.0)		115 358 (38.8)	58 487 (36.4)	19 257 (36.0)	
Black/Brown	198 096 (37.9)	61 450 (35.6)	114 378 (39.0)	22 268 (39.6)		106 312 (35.8)	66 889 (41.7)	19 891 (37.2)	
Other	7237 (1.4)	2135 (1.2)	4191 (1.4)	911 (1.6)		4028 (1.4)	2332 (1.5)	710 (1.3)	
Not reported	120 799 (23.1)	41 269 (23.9)	60 476 (20.6)	19 054 (33.8)		71 345 (24.0)	32 787 (20.4)	13 645 (25.5)	
Region of residence, number (%)					<0.001				<0.001
North	41 961 (8.0)	10 024 (5.8)	27 065 (9.2)	4872 (8.7)		23 149 (7.8)	14 537 (9.1)	3559 (6.7)	
Northeast	104 213 (20.0)	33 220 (19.3)	50 377 (17.2)	20 616 (36.6)		49 733 (16.7)	37 919 (23.6)	12 695 (23.7)	
Center-West	48 864 (9.4)	16 581 (9.6)	28 872 (9.8)	3411 (6.1)		29 169 (9.8)	13 532 (8.4)	4759 (8.9)	
Southeast	257 503 (49.3)	88 817 (51.5)	144 010 (49.1)	24 676 (43.8)		151 595 (51.0)	76 494 (47.7)	25 050 (46.8)	
South	69 590 (13.3)	23 814 (13.8)	43 042 (14.7)	2734 (4.9)		43 380 (14.6)	17 997 (11.2)	7439 (13.9)	
Foreigner	36 (0.0)	17 (0.0)	18 (0.0)	1 (0.0)		17 (0.0)	16 (0.0)	1 (0.0)	
Hospital in the same municipality of residence, number (%)					<0.001				<0.001
Yes	388 304 (74.4)	118 002 (68.4)	227 423 (77.5)	42 879 (76.2)		224 134 (75.5)	116 664 (72.7)	39 772 (74.3)	
No	133 827 (25.6)	54 454 (31.6)	65 943 (22.5)	13 430 (23.9)		72 892 (24.5)	43 815 (27.3)	13 730 (25.7)	
Distance (km) from residence to hospital†	32.0 (18.4–64.1)	35.6 (19.8–77.8)	29.4 (18.0–56.6)	25.8 (14.5–54.7)	<0.001	29.8 (18.1–57.8)	34.1 (19.1–71.9)	34.5 (18.8–75.9)	<0.001

*Includes 11 126 patients with unknown clinical outcome.
†Non-survivors are classified as those whose death was associated with COVID-19, according to the *SIVEP-Gripe* database. Those who had COVID-19 but died due to an unrelated cause are classified under 'Survivor & non-COVID-19 death'. Survivor n=296 002, non-COVID-19 death=1041.
‡Distances (measured in km) are calculated from the centroid of the notification municipality (consistent with municipality of hospitalisation) to the centroid of the municipality of residence, using the South America Lambert Conformal Conic projection.
ICU, intensive care unit.

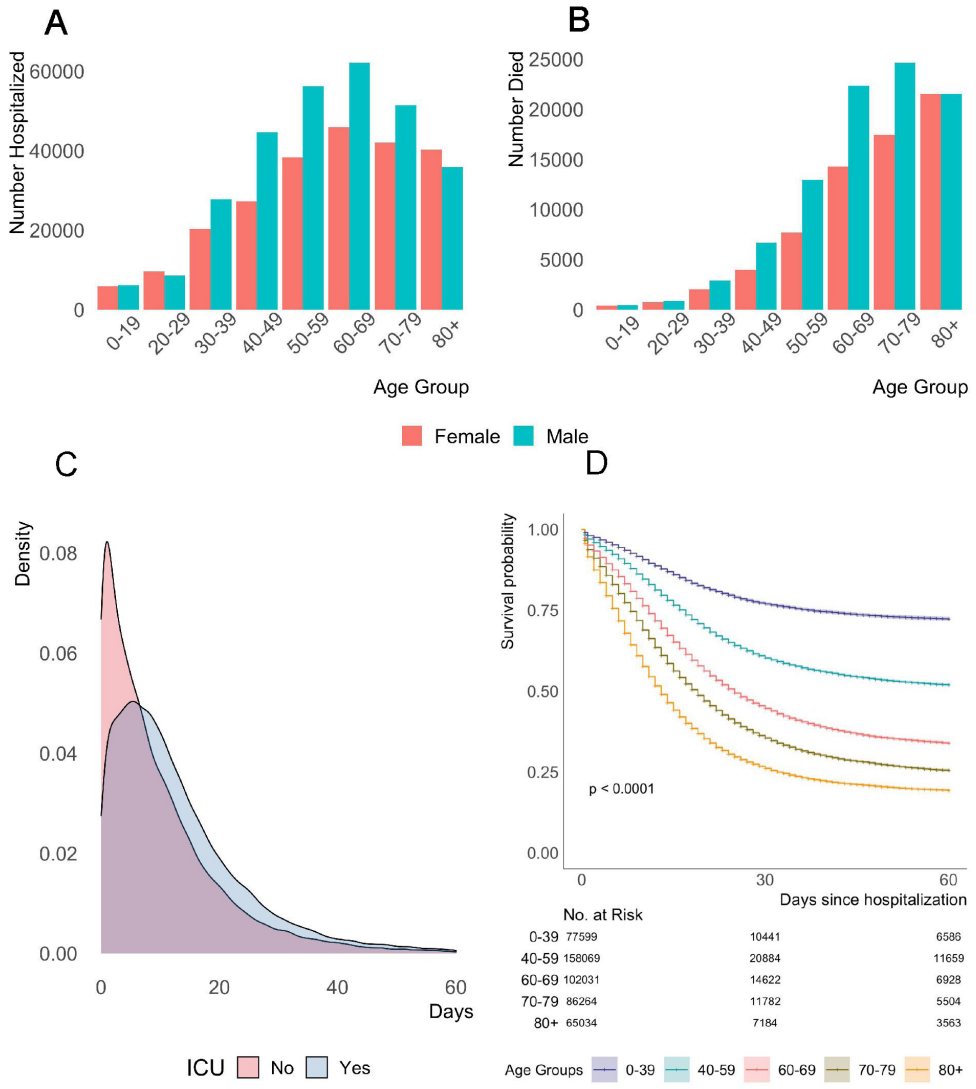

Figure 1 Age distribution of patients, density curves of length of time from hospital admission to death and survival curve 60 days after hospital admission. (A) Age distribution of patients hospitalised. (B) Age distribution of in-hospital deaths. (C) Density of number of days from hospital admission to death up to 60 days after hospital admission, detailed by ICU admission status. (D) Survival curve estimated with Kaplan Meier and considering 60 days from hospital admission. ICU, intensive care unit.

age of 65 years (IQR, 52–76) needed ICU admission. Of all hospitalisations, 37.7% of the patients were White, and 37.9% were Black/Brown. Among survivors, 38.8% were White, while among non-survivors 41.7% were Black/Brown. About 25% of the patients travelled a median of 32.0 km (IQR, 18.6–64.1) to be hospitalised in a municipality different from where they reside (table 1).

Comorbidities were observed in 64.5% of the patients, 74.6% of those who needed ICU admission, 76.8% of non-survivors and 58.5% of the survivors and those whose death was not associated with COVID-19. With the exception of asthma, all comorbidities had a higher prevalence among non-survivors (compared with all patients). The most common comorbidities were chronic cardiovascular disease (34.5% of patients and 43.5% of non-survivors) and diabetes (25.7% of patients and 33.0% of non-survivors). Obesity was reported in 7.4% of the patients and 10.5% of those who needed ICU admission. The most common symptoms were fever, cough, shortness of breath, low oxygen saturation and respiratory distress symptoms (table 2).

The median time from illness onset to hospital admission was 6 days (IQR, 3–9), slightly shorter among non-survivors, 5 days (IQR, 2–8). Mechanical ventilation was needed by 62.2% of all patients, and by 75.6% of those who died. Invasive ventilation was more common in the ICU (44.0%). Oseltamivir, an antiviral medication, was the most common drug used during treatment (15.8% overall, and 17.6% among those in ICU), and the median time from illness onset to treatment was 5 days (IQR, 3–8). Of the patients who needed ICU, 51.8% died from causes associated with COVID-19, and 19.0% remained hospitalised after ICU discharge for 5 days (IQR, 2–10). The median time from illness onset to ICU admission was 7 days (IQR, 3–10), and the medium length of ICU stay was 8 days (IQR, 3–15) for all patients, 9 days (IQR, 4–16) for the deceased. Among the 160 495 patients who died of causes associated with COVID-19 by 14 December,

Table 2 Clinical and radiographic characteristics of patients

Characteristic	All patients (n=522167)*	ICU admission (n=172473)	Non-ICU admission (n=293384)	Not reported (n=56310)	P value	Survivor and non-COVID-19 death (n=297043)	Non-survivor (n=160495)†	Still in the hospital (n=53503)	P value
Any comorbidity, number (%)	336909 (64.5)	128590 (74.6)	179847 (61.3)	28472 (50.6)	<0.001	173828 (58.5)	123265 (76.8)	33318 (62.3)	<0.001
Chronic cardiovascular disease	180370 (34.5)	72196 (41.9)	93574 (31.9)	14600 (25.9)	<0.001	89402 (30.1)	69768 (43.5)	17980 (33.6)	<0.001
Chronic haematologic diseases	4134 (0.8)	1687 (1.0)	2204 (0.8)	243 (0.4)	<0.001	1957 (0.7)	1739 (1.1)	365 (0.7)	<0.001
Chronic hepatic disease	4732 (0.9)	2101 (1.2)	2309 (0.8)	322 (0.6)	<0.001	1924 (0.7)	2368 (1.5)	361 (0.7)	<0.001
Asthma	14567 (2.8)	4947 (2.9)	8639 (2.9)	981 (1.7)	<0.001	9130 (3.1)	3634 (2.3)	1514 (2.8)	<0.001
Diabetes	134391 (25.7)	53717 (31.2)	69078 (23.6)	11596 (20.6)	<0.001	65941 (22.2)	52958 (33.0)	12844 (24.0)	<0.001
Chronic neurological disease	21016 (4.0)	8821 (5.1)	10832 (3.7)	1363 (2.4)	<0.001	8113 (2.7)	10943 (6.8)	1622 (3.0)	<0.001
Chronic lung disease	20140 (3.9)	9249 (5.4)	9483 (3.2)	1408 (2.5)	<0.001	8222 (2.8)	10021 (6.2)	1621 (3.0)	<0.001
Immunodeficiency	13967 (2.7)	5689 (3.3)	7376 (2.5)	902 (1.6)	<0.001	6351 (2.1)	6283 (3.9)	1132 (2.1)	<0.001
Chronic renal disease	21725 (4.2)	10684 (6.2)	9429 (3.2)	1512 (2.9)	<0.001	8149 (2.7)	11491 (7.2)	1743 (3.3)	<0.001
Obesity	38415 (7.4)	18057 (10.5)	17998 (6.1)	2360 (4.2)	<0.001	20993 (7.1)	12765 (8.0)	4005 (7.5)	<0.001
Others‡	144081 (27.6)	58139 (33.7)	74994 (25.6)	10948 (19.4)	<0.001	72598 (24.4)	55866 (34.8)	13042 (24.4)	<0.001
Symptoms, number (%)									
Fever	188572 (64.3)	104650 (60.7)	188572 (64.3)	34789 (61.8)	<0.001	194578 (65.5)	93933 (58.5)	32586 (60.9)	<0.001
Cough	369192 (70.7)	115147 (66.7)	215084 (73.3)	38961 (69.2)	<0.001	219433 (73.9)	105252 (65.6)	36717 (68.6)	<0.001
Sore throat	90487 (17.3)	23531 (13.6)	56653 (19.3)	10303 (18.3)	<0.001	56741 (19.1)	22982 (14.3)	8872 (16.6)	<0.001
Shortness of breath	367917 (70.5)	131799 (76.4)	199805 (68.1)	36313 (64.5)	<0.001	200051 (67.4)	124724 (77.7)	35709 (66.7)	<0.001
Respiratory distress syndrome	296238 (56.7)	107762 (62.5)	163370 (55.7)	25106 (44.7)	<0.001	157412 (53.0)	104555 (65.2)	28046 (52.4)	<0.001
Oxygen saturation <95%	303282 (58.1)	116355 (67.5)	160837 (54.8)	26090 (46.3)	<0.001	156349 (52.6)	111097 (69.2)	29704 (55.5)	<0.001
Diarrhoea	71069 (13.6)	20340 (11.8)	44411 (15.1)	6318 (11.2)	<0.001	44961 (15.1)	17419 (10.9)	7264 (13.6)	<0.001
Vomiting	41974 (8.0)	11950 (6.9)	26177 (8.9)	3847 (6.8)	<0.001	25799 (8.7)	11076 (6.9)	4156 (7.8)	<0.001
Others§	179222 (34.3)	58268 (33.8)	105646 (36.0)	15308 (27.2)	<0.001	112278 (37.8)	45263 (28.2)	18294 (34.2)	<0.001
Chest radiograph, number (%)					<0.001				<0.001
Normal	11816 (2.3)	3403 (2.0)	7782 (2.7)	631 (1.1)		7895 (2.7)	2558 (1.6)	1091 (2.0)	
Interstitial abnormalities	81412 (15.6)	28091 (16.3)	48864 (16.7)	4457 (7.9)		45320 (15.3)	27071 (16.9)	7500 (14.0)	
Other¶	85870 (16.4)	35844 (20.8)	47185 (16.1)	2841 (5.1)		246250 (82.9)	132429 (82.5)	47639 (89.0)	

*Includes 11126 patients with unknown clinical outcome.
†Non-survivors are classified as those whose death was associated with COVID-19, according to the *SIVEP-Gripe* database. Those who had COVID-19 but died due to an unrelated cause are classified under 'Survivor & non-COVID-19 death'. Survivor n=296002, non-COVID-19 death=1041.
‡Other comorbidities that were not specifically asked about in the survey, but self-reported as 'other' include, but are not limited to hypertension, cancer, anaemia, bronchitis, dyslipidaemia and pulmonary emphysema.
§Other symptoms that were not specifically asked about in the surveillance form, but self-reported as 'other' include, but are not limited to loss of taste, loss of smell, myalgia, weakness, body ache, fatigue, exhaustion, tachypnea and syncope.
¶Includes consolidation, mixed and other.
ICU, intensive care unit.

the median time from illness onset to death was 15 days (IQR, 9–24) (table 3). Medium length of hospital stay was 8 days (IQR, 4–17), but longer for those who needed ICU admission, 12 days (IQR, 6–22). The density of time from hospital admission to death is positively skewed, more so for those who did not get admitted to the ICU (figure 1C).

Kaplan Meier curves (figure 1D and online supplemental figure 2) for a period of up to 60 days after hospital admission showed that survival curves were significantly different by age, region, sex, ethnoracial self-classification and ICU admission.

Univariable logistic analysis indicated that the odds of in-hospital death progressively increased with age, and were higher for patients who were male, non-white, from the North and Northeast regions, needed ICU care, were obese and had diabetes and other comorbidities (table 4). The multivariable analysis included 168 936 records (65 670 non-survivors) that had no missing data for covariates. The odds of in-hospital death for males are 1.23 times that of females, and for those in the North and Northeast regions were, respectively, 1.83 and 1.48 times that of patients in the Southeast. The Cox proportional-hazards model included 176 559 records (64 809 non-survivors). Variables associated with in-hospital death were age, sex, ethnoracial self-classification, region, ICU care and various comorbidities. Age, however, had the highest hazard ratios, ranging from 1.67 (95% CI: 1.49 to 1.89) for those aged 20–39 to 5.51 (95% CI: 4.91 to 6.18) for those 80 or older, compared with patients younger than 20 years (table 4).

DISCUSSION

This study described demographic, clinical and radiographic characteristics, treatment, case outcome and risk factors associated with in-hospital death of 522 167 patients hospitalised with confirmed COVID-19 in Brazil. Results show that 56.7% were discharged, 0.002% died of other causes, 30.7% died of causes associated with COVID-19 and 10.2% remained in the hospital as of 14 December. Patients were mostly older than 40 years, predominantly from the Southeast region, with about one-fourth needing to travel to a different municipality for hospitalisation. At least one comorbidity was present in 64.5% of patients and in 76.8% of the non-survivors. From illness onset, the median time to hospital and ICU admission was 6 and 7 days, respectively; 15 days to death (17 to those admitted to the ICU) and 15 days to hospital discharge (18 days to those admitted to the ICU). Risk factors for in-hospital death were older age, being male, of Black/Brown ethnoracial self-classification, living in the North or Northeast regions, with a history of ICU admission and various co-morbidities.

Our results can be analysed in light of findings from other countries. The use of mechanical ventilation was higher in Brazil (62.2% among all patients, 75.6% of the non-survivors) compared with patterns described for China (ranging from 17.2% to 38.7% of patients),[8–10] and Germany (17% of patients),[11] but lower than Italy (81.7% of all patients).[12] While ICU mortality in Italy was 26%,[12] in Brazil, it was 51.8%. In Brazil, 33.0% of hospitalised patients were admitted to the ICU, against 16% in Italy,[13] and 19% in France.[14] In-hospital death was observed in 18.1% of patients in France,[14] 22% in Germany[11] and 30.7% in Brazil. The time from illness onset to hospitalisation in China[9] was 11 days (IQR, 8–14), but much shorter in Brazil, 6 days (IQR, 3–9). The length of hospital stay, however, was about 4 days longer in China.[9 15] These comparisons need to be taken with caution. First, studies from China had a smaller sample size, and regional variability is very large, as reported for France.[14] In Brazil, for example, in-hospital death varied from 25.9% in the South region to 36.4% in the Northeast, and ICU mortality from 48.0% in the Southeast to 66.5% in the North. The time from illness to hospitalisation was also longer in the North and Center-West regions, 7 days (IQR, 4–10).

Our results confirm previous findings regarding symptoms and comorbidities. Hypertension, a very common comorbidity in China[9] could not be measured from our data, but over one-third of the adult population in Brazil has that condition.[16] In Brazil, 35.5% of the patients reported no comorbidities, while in New York City, this number was 6.1%,[17] and in China, it was 52%.[9] Diabetes was reported in 19% of patients in China,[9] 33.8% in New York City[17] and 25.7% in Brazil. Part of these differences reflects the disease burden in each locality, but also the lack of standardised data collection (eg, conditions systematically collected in one country and only reported in the 'other' category in another country).

The observed associations of age, sex, obesity and diabetes with in-hospital death corroborate previous findings.[5 6 14] The higher risk among non-white patients was previously reported in Brazil, the UK and the USA.[18–22] In Brazil, this reflects structural inequalities that made large fractions of the population more vulnerable to COVID-19 (eg, people living in areas with precarious infrastructure, overcrowded households, regions with low supply of physicians and hospital services and who depend on informal labour).[23 24] Those inequalities are also captured by a higher HR in the North and Northeast regions, where Brazil consistently reports worse socioeconomic indicators.[25] Currently, the North region has the lowest rates of hospital beds, ICU beds and physicians per person.[26] Indeed, the region had the worst indicators in terms of mortality and time to hospitalisation, and patients who were hospitalised in a municipality different from the one where they live had to travel 122.0 km (IQR, 58.3–258.6), while those in the Southeast travelled 22.3 km (IQR, 16.1–36.3). Hospitalisation in a different municipality occurs when the place of residence has no hospitals, has no available hospital beds or when the closest hospital is actually outside the municipality of residence. In Brazil, the size of municipalities varies widely: 23% have 5000 residents or less, and 5% have 100 000 or more residents. Of the 5570 municipalities, 37% and 75% have no hospitals and no ICU care, respectively. A regionalisation process guarantees that all the population has access to hospital care.[27] However, when hospitals reach capacity, as was observed in several cities in

Table 3 Treatment and outcomes of patients

Variable	All patients (n=522 167)*	ICU admission (n=172 473)	Non-ICU admission (n=293 384)	Not reported (n=56 310)	P value	Survivor and non-COVID-19 death (n=297 043)	Non-survivor (n=160 495)	Still in the hospital (n=53 503)	P value
Treatment with drugs, number (%)					<0.001				<0.001
Oseltamivir	82 659 (15.8)	30 341 (17.6)	47 317 (16.1)	5001 (8.9)		50 091 (16.9)	27 192 (16.9)	4242 (7.9)	
Zanamivir	492 (0.1)	152 (0.1)	303 (0.1)	37 (0.1)		298 (0.1)	128 (0.1)	56 (0.1)	
Other	5008 (1.0)	1480 (0.9)	3243 (1.1)	285 (0.5)		3029 (1.0)	1118 (0.7)	701 (1.3)	
Mechanical ventilation, number (%)					<0.001				<0.001
Invasive	90 189 (17.3)	75 915 (44.0)	12 019 (4.1)	2255 (4.0)		17 263 (5.8)	66 652 (41.5)	5238 (9.8)	
Non-invasive	234 554 (44.9)	65 281 (37.9)	157 913 (53.8)	11 360 (20.2)		148 930 (50.1)	54 652 (34.1)	25 925 (48.5)	
ICU admission, number (%)	172 473 (33.0)	172 473 (100.0)	–	–	–	65 102 (21.9)	89 264 (55.6)	15 614 (29.2)	<0.001
Remained hospitalised after ICU discharge, number (%)	32 770 (19.0)	32 770 (19.0)	–	–	–	27 775 (42.7)	3243 (3.6)	1303 (8.4)	<0.001
Median length (IQR), days	5 (2–10)	5 (2–10)	–	–	–	5 (2–9)	7 (2–16)	72 (21–139)	<0.001
Median times (IQR), days									
Illness onset to treatment with drugs	5 (3–8)	5 (3–8)	6 (3–9)	6 (3–8)	<0.001	6 (3–9)	5 (2–8)	6 (3–9)	<0.001
Illness onset to hospitalisation	6 (3–9)	6 (3–9)	6 (3–10)	6 (2–9)	<0.001	7 (3–10)	5 (2–8)	6 (3–10)	<0.001
Illness onset to ICU admission	7 (3–10)	7 (3–10)	–	–	–	7 (4–10)	6 (3–10)	7 (3–10)	<0.001
Hospital admission to ICU admission	0 (0–1)	0 (0–1)	–	–	–	0 (0–1)	0 (0–1)	0 (0–0)	<0.001
Illness onset to death	15 (9–24)	17 (10–25)	13 (7–21)	12 (7–20)	<0.001	–	15 (9–24)	–	–
Illness onset to hospital discharge	15 (11–20)	18 (13–27)	14 (10–18)	16 (11–21)	<0.001	15 (11–20)	–	–	–
Hospital admission to death	9 (4–16)	10 (5–18)	7 (2–14)	5 (1–13)	<0.001	–	9 (4–16)	–	–
Hospital admission to ICU discharge	9 (4–17)	9 (4–17)	–	–	–	7 (4–14)	10 (5–10)	6 (2–14)	<0.001
ICU admission to death	9 (4–16)	9 (4–16)	–	–	–	–	9 (4–16)	–	–
Median length hospital stay (IQR), days	8 (4–17)	12 (6–22)	7 (4–13)	8 (3–18)	<0.001	7 (4–12)	9 (4–16)	79 (23–157)	<0.001
Median length ICU stay (IQR), days	8 (3–15)	8 (3–15)	–	–	–	6 (3–12)	9 (4–16)	4 (2–11)	<0.001
Clinical outcomes as of 14 December 2020, number (%)					<0.001				–
Cured and discharged from hospital	296 002 (56.7)	64 578 (37.4)	202 042 (68.9)	29 382 (52.2)		296 002 (99.7)	–	–	
Death due to other causes	1041 (0.2)	524 (0.3)	443 (0.2)	74 (0.1)		1041 (0.4)	–	–	
Death associated with COVID-19	160 495 (30.7)	89 264 (51.8)	53 282 (18.2)	17 949 (31.9)		–	160 495 (100.0)	–	
Still in the hospital	53 503 (10.3)	15 614 (9.1)	30 963 (10.6)	6926 (12.3)		–	–	53 503 (100.0)	

*Includes 11 126 patients with unknown clinical outcome.
†Non-survivors are classified as those whose death was associated with COVID-19, according to the *SIVEP-Gripe* database. Those who had COVID-19 but died due to an unrelated cause are classified under 'Survivor & non-COVID-19 death'. Survivor n=296 002, non-COVID-19 death=1041.
ICU, intensive care unit.

Table 4 ORs and HRs for death among hospitalised patients with confirmed COVID-19

Variables	Univariable OR* (95% CI)	P value†	Multivariable OR (95% CI) n=168 936	P value†	HR (95% CI) for death within 60 days of hospitalisation n=176 559
Age (reference 0–19)					
20–39	1.35 (1.26 to 1.46)	<0.001	1.66 (1.45 to 1.91)	<0.001	1.67 (1.48 to 1.89)
40–59	2.94 (2.74 to 3.15)	<0.001	2.70 (2.37 to 3.09)	<0.001	2.21 (1.97 to 2.48)
60–69	6.76 (6.30 to 7.26)	<0.001	5.15 (4.52 to 5.88)	<0.001	3.05 (2.72 to 3.43)
70–79	11.05 (10.30 to 11.86)	<0.001	8.24 (7.24 to 9.42)	<0.001	3.90 (3.48 to 4.38)
≥80	17.58 (16.37 to 18.88)	<0.001	14.52 (12.74 to 16.59)	<0.001	5.51 (4.91 to 6.18)
Sex (reference female)					
Male	1.10 (1.09 to 1.11)	<0.001	1.23 (1.20 to 1.26)	<0.001	1.09 (1.07 to 1.10)
Ethnoracial self-classification (reference White)					
Black/Brown	1.25 (1.24 to 1.27)	<0.001	1.18 (1.15 to 1.22)	<0.001	1.08 (1.06 to 1.10)
Other	1.18 (1.12 to 1.25)	<0.001	1.05 (0.95 to 1.16)	0.309	1.02 (0.96 to 1.10)
Not reported	0.9 (0.89 to 0.92)	<0.001	0.77 (0.74 to 0.80)	<0.001	0.79 (0.77 to 0.81)
Region (reference Southeast)					
South	0.85 (0.83 to 0.87)	<0.001	0.89 (0.87 to 0.92)	<0.001	0.91 (0.89 to 0.93)
Center-West	0.96 (0.94 to 0.98)	<0.001	1.04 (1.00 to 1.08)	0.049	1.00 (0.97 to 1.03)
North	1.31 (1.28 to 1.34)	<0.001	1.83 (1.75 to 1.92)	<0.001	1.34 (1.30 to 1.39)
Northeast	1.61 (1.58 to 1.64)	<0.001	1.48 (1.43 to 1.55)	<0.001	1.10 (1.07 to 1.12)
ICU	5.21 (5.14 to 5.28)	<0.001	5.20 (5.08 to 5.32)	<0.001	1.78 (1.75 to 1.81)
Obesity	0.91 (0.88 to 0.93)	<0.001	1.23 (1.18 to 1.27)	<0.001	1.07 (1.04 to 1.10)
Diabetes	1.32 (1.30 to 1.35)	<0.001	1.18 (1.15 to 1.21)	<0.001	1.08 (1.07 to 1.10)
Asthma	0.59 (0.56 to 0.61)	<0.001	0.81 (0.77 to 0.86)	<0.001	0.88 (0.84 to 0.92)
Chronic liver disease	1.87 (1.76 to 1.99)	<0.001	1.74 (1.59 to 1.90)	<0.001	1.33 (1.26 to 1.40)
Chronic neurological disease	2.12 (2.06 to 2.19)	<0.001	1.65 (1.58 to 1.73)	<0.001	1.18 (1.15 to 1.21)
Chronic lung disease	1.92 (1.86 to 1.99)	<0.001	1.46 (1.40 to 1.53)	<0.001	1.16 (1.13 to 1.19)
Immunodeficiency	1.53 (1.47 to 1.58)	<0.001	1.93 (1.83 to 2.04)	<0.001	1.26 (1.22 to 1.31)
Chronic kidney disease	2.23 (2.16 to 2.30)	<0.001	1.70 (1.63 to 1.78)	<0.001	1.17 (1.14 to 1.21)

*The N varies for univariable OR, depending on the number of missing values for each variable.
†P value from Wald test.
ICU, intensive care unit.

Brazil in late April and May, municipalities without hospitals and ICU units are unable to provide proper care, which may have contributed to higher COVID-19 mortality. Therefore, risk factors for in-hospital mortality due to COVID-19 expose local and structural inequalities.

This study has some limitations. First, we used administrative records captured in structured surveillance forms. Those lack details available in hospital medical records and may have accuracy and completeness problems. In addition, it limits the types of comorbidities and symptoms reported, as those listed under the 'other' category were not systematically collected from all cases (eg, loss of taste and smell). Second, we did not have access to laboratory results other than COVID-19 tests (eg, complete blood count). While this does not change any of our results, they would allow for a better characterisation of the clinical course of the disease. Third, 23.1% of patients did not report information on ethnoracial self-classification, 10.8% did not have information on ICU admission and for 2.1%, there was no information on clinical outcome. This is not uncommon in the analysis of administrative records.[22] Here, we report all records and included an additional category (ethnoracial self-classification not reported) in the risk factor analysis.

Despite these limitations, this study provides a comprehensive description of characteristics, outcomes and risk factors for mortality of patients hospitalised with COVID-19 in Brazil, and the largest cohort of patients so far analysed (n=522 167). Results shed light on commonalities and

differences between Brazil and other countries affected by COVID-19, and highlight inequalities in disease outcomes. Most importantly, our results could be used to inform coordinated actions to target those who currently bear the highest morbidity and mortality burden. Brazil has a network of almost 270 000 community health workers that reach out to about 70% of the Brazilian population. These agents could actively identify vulnerable people who face higher risk of mortality, could act as agents of information to sensitise the population and boost adherence to control measures (eg, use of masks) and could continue to deliver community-based primary care services that have been, for the most part, interrupted by the pandemic. These agents will also be important to support the delivery of vaccination to the most vulnerable. Leveraging and strengthening the existing network of primary healthcare is paramount to contain the sustained and unequal burden of COVID-19 in Brazil.

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